expressed as AUC and outcome. **Methods:** All children, transplanted between 2001–2006, receiving intravenous BU as part of a myeloablative regimen, from whom AUC measurements were available, were included. Patients were separated into five percentiles based on total AUC. The association with the primary endpoints EFS (event defined as dead, graft-failure or relapse) and survival as well as the secondary endpoints (acute Graft-versus-Host Disease grade 2–4; aGvHD, and Veno-occlusive Disease: VOD) were tested using uni- and multivariate Cox regression analysis. The lowest AUC group was used as index group. **Results:** 102 patients were included (46 malignant indications; 56 non-malignant indications). Median age at transplantation was 3.1 years (range 0.2 to 21 years). The overall EFS and survival were 68% and 72% respectively. In multivariate analyses a total AUC between 72,500–80,000μg•h/l was associated with highest EFS (85%, p = 0.029, table). Other factors influencing EFS were HLA-disparity and age at SCT. Similar associations were found for survival. aGvHD occurred in 16% of patients and was most frequently seen in the highest AUC group 35% (p = 0.041, table). VOD was noted more frequent in the higher AUC, but not significant (p = 0.164). The once daily dosing versus 4-times daily did not influence any of the results. Above an AUC of 72.500 μg•h/l, no graft-failure was note and only 2 relapses (11%) were note. While under 72.500 μg•h/l, 9 graft-failure and relapses were seen (31%).

In conclusion a total AUC between 72,500–80,000 μg•h/l is associated with highest EFS in malignants as well as in non-malignant disease. Higher AUC was associated with more toxicity negatively influencing EFS, while lower AUC was associated with more relapse/graft failure. Once daily dosing might be a practical alternative to 4-times daily. Dosing of busulfan in children should be targeted by therapeutic drug monitoring to a small therapeutic range to improve EFS.

Multivariate analysis of primary and secondary endpoint: EFS en GvHD

	EFS			GvHD		
	P	HR	CI-95%	P	OR	CI-95%
AUC 0–55.000		1			1	
AUC 55,000–65,000	0.320	0.60	0.22–1.64	0.920	0.86	0.05–15.8
AUC 65,000–72,500	0.537	0.72	0.25–2.05	0.330	3.41	0.29–40.2
AUC 72,500–80,000	0.029	0.20	0.05–0.85	0.177	5.58	0.46–67.7
AUC 80,000–120,000	0.378	0.59	0.18–1.92	0.041	12.55	1.10–143
Malign vs non-malignant				0.080	5.13	0.82–31.9
HLA disparity	0.001	3.79	1.72–8.35	0.197	0.38	0.09–1.65
Melphalan				0.541	1.71	0.31–9.43
Sero-therapy	0.244	2.42	0.55–10.7			
Age	0.001	1.12	1.05–1.19			

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INFLUENCE OF DONOR AGE ON RISK OF CHRONIC GVHD IN SEX-MISMATCHED PEDIATRIC ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANT

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Background: Donor age, donor/recipient sex mismatch, and donor parity are considered to be significant risk factors for the development of acute and chronic graft versus host disease. Most reports indicate that female donors into male (F-M) recipients confer the greatest risk. Female donor alloimmunization to minor histocompatibility antigens encoded by the Y-chromosome is thought to develop through sexual exposure and/or parity and at least partially explain the increased risk of GVHD seen in F-M transplants. There are no studies that evaluate this association when a young female serves as donor. **Methods:** Data from 43 male to male (M-M) and 38 female to male (F-M) sibling donor hematopoietic transplants performed at our institution from 1998–2006 was collected and analyzed. Twenty three F-M transplants used female donors less or equal to 12 years old. Age range and mean age for each group was as follows: M-M (1–23 years, 11 years), F-M with donor less than or equal to 12 years old (0.2–16 years, 7 years), and F-M with donor over 12 years old (9–33 years, 15 years). The majority of patients in both groups had hematologic malignancies, was fully matched, and received Cyclosporine and Methotrexate as GVHD prophylaxis. Outcomes between patients with female donors less or equal to 12 years old were compared to those of patients with female donors more than 12 years old, using patients with M-M transplant as baseline. Only patients with aGVHD grade II-IV were included in analysis. Patients with death in the first 100 days were not included in the cGVHD analysis. **Results:** As reported from adult literature, increased risk of chronic GVHD (RR = 3.3, 95% CI = 1.47–7.38, p = 0.006) was observed in F-M transplant from older female donor when compared to M-M (RR = 1). However, no significant increase in risk of acute or chronic GVHD (RR = 0.76, p = 0.5; RR = 0.93, p = 0.9) was observed when the subgroup including young female donors was compared to M-M (RR = 1). Furthermore, no significant difference in relapse or transplant related mortality rates in the first 100 days were observed. **Conclusion:** This data suggests that the increased risk for chronic GVHD observed in adult sex-mismatched allogenic transplants may be related to donor alloimmunity and may not be present when a young female serves as donor.

Effect of donor-recipient sex match on Grade II-IV aGVHD, cGVHD, Disease Relapse and Death in first 100 days

		RR	95% CI	P value
aGVHD				
M-M (n = 43)	11	1	NA	NA
F-M (all combined)	10	1.02	0.60–1.72	0.93
F-M <12 (n = 23)	4	0.76	0.29–1.78	0.5
F-M >13 (n = 15)	6	1.61	0.68–3.82	0.29
cGVHD				
M-M (n = 40)	4	1	NA	NA
F-M (all combined)	8	1.52	0.93–2.48	0.14
F-M <12 (n = 22)	2	0.93	0.28–3.05	0.9
F-M >13 (n = 14)	6	3.3	1.47–7.38	0.006
Relapse				
M-M (n = 43)	12	1	NA	NA
F-M <12 (n = 23)	4	0.65	0.26–1.65	0.34
F-M >13 (n = 15)	4	0.95	0.35–2.57	0.92
Death				
M-M (n = 43)	3	1	NA	NA
F-M <12 (n = 23)	1	0.7	0.12–3.97	0.7
F-M >13 (n = 15)	1	0.92	0.16–5.58	0.97

NA= Not applicable.

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ACUTE GRAFT-VERSUS-HOST DISEASE (AGVHD) IN UNRELATED CORD BLOOD TRANSPLANTATION (UCBT): SINGLE INSTITUTION EXPERIENCE, JULY 1996 – JUNE 2007

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UCBT has been associated with a lower incidence of GVHD when compared to unrelated transplant using adult donors. However, the characteristics (sites, time to onset, course, and tolerability) of GVH following UCBT has not been as clearly elucidated. We review GVH in 81 consecutive UCBT treated on a single therapeutic trial with consistenet GVH prophylaxis. 13 patients were unevaluable based on death prior to UCB infusion (2), death prior to engraftment (7), or graft rejection (4). Thus, 68 patients were evaluable for AGVHD (41 male, 27 female; median age 6.8 yr (range, 0.3–24.4 yr); median weight 22 Kg (range, 5.35–82.9 Kg)). Diagnoses included leukemia in 75% (63% ALL, 25% AML, 12% CML or JMML), MDS 3%, lymphoma 1%, metabolic disorders 6%, immune/genetic disorders 9%, and aplastic anemia 6%. Acute leukemia disease status at UCBT was CR1 24%, CR2